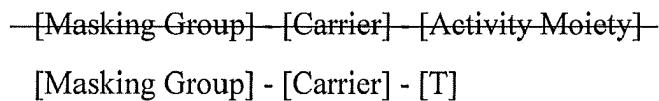


Amendments to and listing of the claims:

Please *amend claims 89-98 and 122*, without prejudice, as shown below in the following listing of all claims ever presented. The following listing of claims replaces all prior versions thereof.

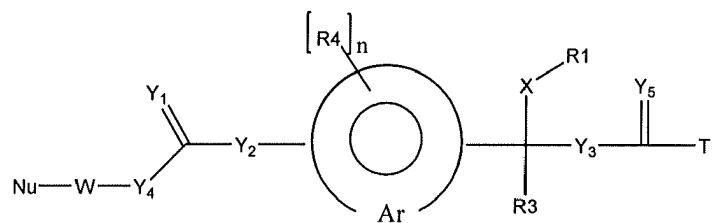
1-88. (Canceled)

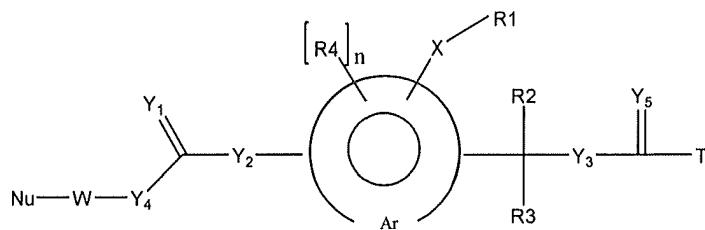
89. (Currently amended) A polymeric cascade prodrug or corresponding linker reagent comprising a compound having the general formula:



wherein the active moiety represents a moiety selected from the group consisting of amine-containing biologically active drugs and leaving groups T represents D or A, wherein D represents an amine-containing biologically active moiety and A represents a leaving group, wherein the masking group comprises at least one nucleophile, and wherein the masking group is different from the carrier.

90. (Currently amended) The polymeric cascade prodrug or corresponding linker reagent according to claim 89, wherein the prodrug or corresponding linker reagent corresponds to a structure selected from the general formula I and II:





wherein T represents D or A; D represents a residue of an amine-containing biologically active moiety; A represents a leaving group; X represents a spacer moiety; Y₁ and Y₂ each independently represent O, S or NR₆; Y₃ represents O or S; Y₄ represents O, NR₆ or -C(R₇)(R₈); R₃ represents a moiety selected from the group consisting of hydrogen, substituted or unsubstituted linear, branched or cyclical alkyl or heteroalkyl groups, aryls, substituted aryls, substituted or unsubstituted heteroaryls, cyano groups, nitro groups, halogens, carboxy groups, carboxyalkyl groups, alkylcarbonyl groups or carboxamidoalkyl groups; R₄ represents a moiety selected from the group consisting of hydrogen, substituted or unsubstituted linear, branched or cyclical alkyls or heteroalkyls, aryls, substituted aryls, substituted or unsubstituted heteroaryl, substituted or unsubstituted linear, branched or cyclical alkoxy, substituted or unsubstituted linear, branched or cyclical heteroalkyloxy, aryloxy or heteroaryloxy, cyano groups and halogens; R₇ and R₈ are each independently selected from the group consisting of hydrogen, substituted or unsubstituted linear, branched or cyclical alkyls or heteroalkyls, aryls, substituted aryls, substituted or unsubstituted heteroaryls, carboxyalkyl groups, alkylcarbonyl groups, carboxamidoalkyl groups, cyano groups, and halogens; R₆ represents a group selected from hydrogen, substituted or unsubstituted linear, branched or cyclical alkyls or heteroalkyls, aryls, substituted aryls and substituted or unsubstituted heteroaryls; R₁ represents a polymer; W represents a group selected from substituted or unsubstituted linear, branched or cyclical alkyls, aryls, substituted aryls, substituted or unsubstituted linear, branched or cyclical heteroalkyls, substituted or unsubstituted heteroaryls; Nu represents a nucleophile; n represents zero or a positive integer; and Ar represents a multi-substituted aromatic hydrocarbon or multi-substituted aromatic heterocycle.

91. (Currently amended) The prodrug according to claim 89, wherein the active moiety T represents D and the ecomprises an amine-containing biologically active drug moiety is selected from the group consisting of small molecule biologically active agents and biopolymers.

92. **(Currently amended)** The prodrug according to claim 90, wherein ~~the residue of an T represents D and the amine-containing biologically active moiety represented by D~~ comprises a biopolymer selected from the group consisting of proteins, polypeptides, oligonucleotides and peptide nucleic acids.

93. **(Currently amended)** The prodrug according to claim 91, wherein the biologically active moiety comprises a biopolymer selected from the group consisting of proteins, polypeptides, oligonucleotides and peptide nucleic acids.

94. **(Currently amended)** The prodrug according to claim 89, wherein the biologically active moiety comprises a polypeptide selected from the group consisting of ACTH, adenosine deaminase, agalsidase, albumin, alfa-1 antitrypsin, alfa-1 proteinase inhibitor, alteplase, anistreplase, ancrod serine protease, antibodies, antithrombin III, antitrypsins, aprotinin, asparaginases, biphalin, bone-morphogenic proteins, calcitonin, collagenase, DNase, endorphins, enfuvirtide, enkephalins, erythropoietins, factor VIIa, factor VIII, factor Villa, factor IX, fibrinolysin, fusion proteins, follicle-stimulating hormones, granulocyte colony stimulating factor, galactosidase, glucagon, glucagon peptides, glucocerebrosidase, granulocyte macrophage colony stimulating factor, phospholipase-activating protein, gonadotropin chorionic, hemoglobins, hepatitis B vaccines, hirudin, hyaluronidases, iduronidase, immune globulins, influenza vaccines, interleukins, IL-1 receptor antagonist, insulins, interferons, keratinocyte growth factor, transforming growth factors, lactase, leuprolide, levothyroxine, luteinizing hormone, lyme vaccine, natriuretic peptide, pancrelipase, papain, parathyroid hormone, PDGF, pepsin, platelet activating factor acetylhydrolase, prolactin, protein C, octreotide, secretin, sermorelin, superoxide dismutase, somatropins, somatostatin, streptokinase, sucrase, tetanus toxin fragment, tilactase, thrombins, thymosin, thyroid stimulating hormone, thyrotropin, tumor necrosis factor, TNF receptor-IgG Fc, tissue plasminogen activator, TSH, urate oxidase, urokinase, vaccines, and plant proteins.

95. **(Currently amended)** The prodrug according to claim 89, wherein the biologically active moiety comprises a protein prepared by recombinant DNA technology.

96. **(Currently amended)** The prodrug according to claim 89, wherein the biologically active moiety comprises a protein selected from the group consisting of antibody fragments, single chain binding proteins, catalytic antibodies and fusion proteins.

97. **(Currently amended)** The prodrug according to claim 89, wherein the biologically active moiety comprises a protein selected from the group consisting of antibodies, calcitonin, G-CSF, GM-CSF, erythropoietins, hemoglobins, interleukins, insulins, interferons, SOD, somatropin, TNF, TNF-receptor-IgC Fc, and glucagon peptides.

98. **(Currently amended)** The prodrug according to claim 90, wherein the ~~residue of an~~ amine-containing biologically active moiety represented by D comprises a protein selected from the group consisting of antibodies, calcitonin, G-CSF, GM-CSF, erythropoietins, hemoglobins, interleukins, insulins, interferons, SOD, somatropin, TNF, TNF-receptor-IgC Fc, and glucagon peptides.

99. (Previously presented) The prodrug according to claim 91, wherein the amine-containing biologically active drug comprises a small molecule biologically active agent having at least one primary or secondary amino group selected from the group consisting of central nervous system-active agents, anti-infective agents, anti-neoplastic agents, antibacterial agents, anti-fungal agents, analgesic agents, contraceptive agents, anti-inflammatory agents, steroidal agents, vasodilating agents, vasoconstricting agents, and cardiovascular agents.

100. (Previously presented) The prodrug according to claim 91, wherein the amine-containing biologically active drug comprises a small molecule biologically active agent selected from the group consisting of daunorubicin, doxorubicin, idarubicin, mitoxantron, aminoglutethimide, amantadine, diaphenylsulfon, ethambutol, sulfadiazin, sulfamerazin, sulfamethoxazol, sulfalen,

clinafloxacin, moxifloxacin, ciprofloxaxin, enoxacin, norfloxacin, neomycin B, sprectinomycin, kanamycin A, meropenem, dopamin, dobutamin, lisinopril, serotonin, acivicin and carbutamid.

101. (Previously presented) The polymeric cascade prodrug or corresponding linker reagent according to claim 90, wherein each R4 independently represents a substituent selected from the group consisting of hydrogen, methyl, ethyl, ethoxy, methoxy, linear alkyls having three or more carbon atoms, cycloalkyls, branched alkyls and C₁₋₆ heteroalkyls.

102. (Previously presented) The polymeric cascade prodrug or corresponding linker reagent according to claim 90, wherein R1 represents a polymer selected from the group consisting of polyalkyloxy polymers, dextran, chitosan, hyaluronic acid and derivatives thereof, alginate, xylan, mannan, carrageenan, agarose, cellulose, starch, hydroxyethyl starch, carbohydrate-based polymers, polyvinyl alcohols, polyoxazolines, polyanhydrides, poly(ortho esters), polycarbonates, polyurethanes, polyacrylic acids, polyacrylamides, polyacrylates, polymethacrylates, polyorganophosphazenes, polysiloxanes, polyvinylpyrrolidone, polycyanoacrylates, polyesters, polyiminocarbonates, polyaminoacids, collagen, gelatin, copolymers, grafted copolymers, cross-linked polymers, and block copolymers thereof.

103. (Previously presented) The polymeric cascade prodrug or corresponding linker reagent according to claim 90, wherein R1 represents a hydrogel.

104. (Previously presented) The polymeric cascade prodrug or corresponding linker reagent according to claim 90, wherein R1 represents a branched or hyperbranched polymer.

105. (Previously presented) The polymeric cascade prodrug or corresponding linker reagent according to claim 90, wherein R1 represents a dendrimer or dense star polymer.

106. (Previously presented) The polymeric cascade prodrug or corresponding linker reagent according to claim 90, wherein R1 represents a biopolymer.

107. (Previously presented) The polymeric cascade prodrug or corresponding linker reagent according to claim 90, wherein R1 represents a protein.

108. (Previously presented) The polymeric cascade prodrug or corresponding linker reagent according to claim 107, wherein the protein is selected from the group consisting of albumin, antibodies, fibrin, casein and plasma proteins.

109. (Previously presented) The polymeric cascade prodrug or corresponding linker reagent according to claim 90, wherein R1 further includes one or more biologically active substances bound to the polymer.

110. (Previously presented) The polymeric cascade prodrug or corresponding linker reagent according to claim 90, wherein R1 has at least one functional group for linkage to X, and wherein the at least one functional group is selected from the group consisting of carboxylic acid and activated derivatives thereof, amino groups, maleimide, thiol, sulfonic acid and derivatives thereof, carbonate and derivatives thereof, carbamate and derivatives thereof, hydroxyl, aldehyde, ketone, hydrazine, isocyanate, isothiocyanate, phosphoric acids and derivatives thereof, phosphonic acids and derivatives thereof, haloacetyls, alkyl halides, acryloyls, arylating agents, hydroxylamines, disulfides, vinyl sulfones, vinyl ketones, diazoalkanes, diazoacetyl compounds, epoxide, oxirane, and aziridine.

111. (Previously presented) The polymeric cascade prodrug or corresponding linker reagent according to claim 110, wherein the at least one functional group is selected from the group consisting of thiol, maleimide, amino groups, carboxylic acid and derivatives thereof, carbonate and derivatives thereof, carbamate and derivatives thereof, aldehyde, and haloacetyls.

112. (Previously presented) The polymeric cascade prodrug or corresponding linker reagent according to claim 110, wherein the bond formed between X and the at least one functional group is selected from the group consisting of disulfide, S-succinimido, amide, amino,

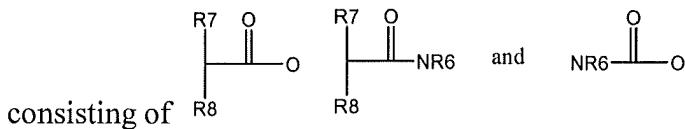
carboxylic ester, sulphonamide, carbamate, carbonate, oxime, hydrazone, urea, thiourea, phosphate, and phosphonate.

113. (Previously presented) The polymeric cascade prodrug or corresponding linker reagent according to claim 110, wherein the bond formed between X and the at least one functional group is selected from the group consisting of S-succinimido, amide, carbamate, and urea.

114. (Previously presented) The polymeric cascade prodrug linker reagent according to claim 89, wherein the active moiety comprises a leaving group selected from the group consisting of chloride, bromide, fluoride, nitrophenoxy, imidazolyl, N-hydroxysuccinimidyl, N-hydroxybenzotriazolyl, N-hydroxyzabenzotriazolyl, pentafluorophenoxy and N-hydroxysulfosuccinimidyl.

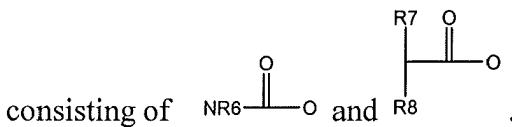
115. (Previously presented) The polymeric cascade prodrug or corresponding linker reagent

according to claim 90, wherein $\text{Y}_4-\text{Y}_2-\text{Y}_1$ represents a moiety selected from the group



116. (Previously presented) The polymeric cascade prodrug or corresponding linker reagent

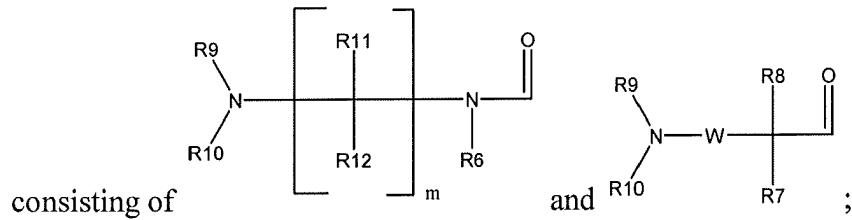
according to claim 90, wherein $\text{Y}_4-\text{Y}_2-\text{Y}_1$ represents a moiety selected from the group



117. (Previously presented) The polymeric cascade prodrug or corresponding linker reagent according to claim 90, wherein R6 represents an additional Nu-W.

118. (Previously presented) The polymeric cascade prodrug or corresponding linker reagent

according to claim 90, wherein $\text{Nu}-\text{W}-\text{Y}_4$  represents a structure selected from the group



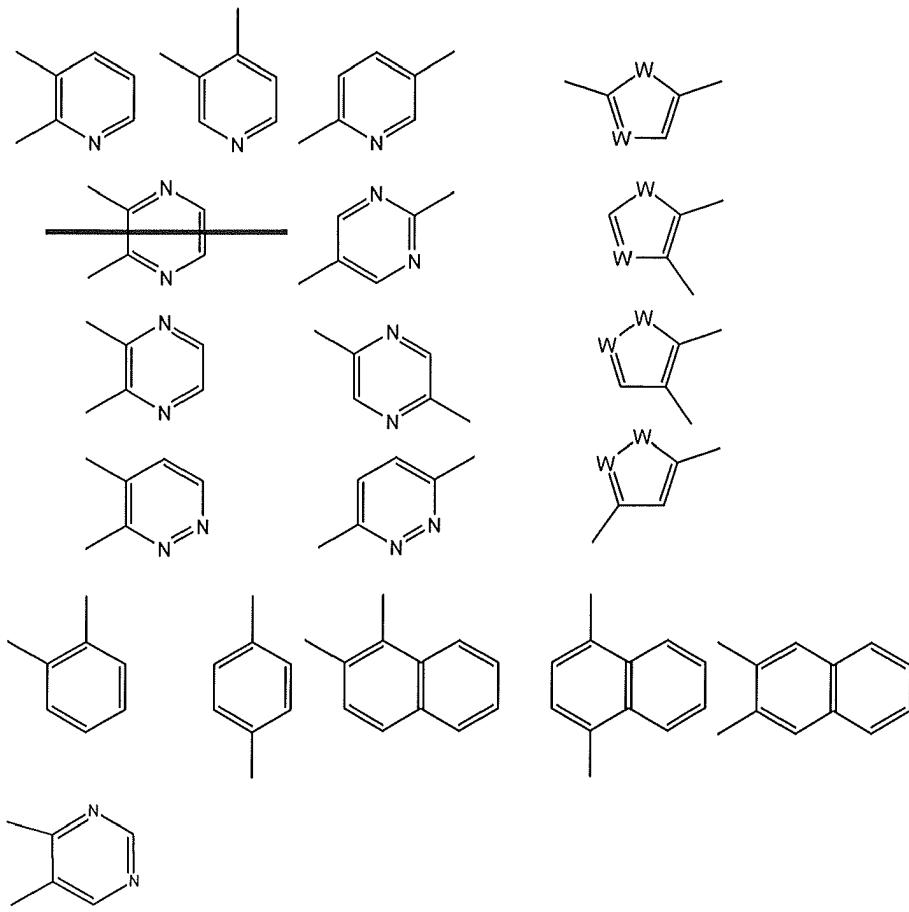
wherein R9, R10, R11 and R12 each independently represent a moiety selected from the group consisting of hydrogen, substituted or non- substituted alkyls or heteroalkyls, and substituted or non-substituted aryls or heteroaryls, and m represents an integer of 2 to 10.

119. (Previously presented) The polymeric cascade prodrug or corresponding linker reagent according to claim 118, wherein R9, 10, R11 and R12 each independently represent a moiety selected from the group consisting of hydrogen and substituted or non-substituted alkyls.

120. (Previously presented) The polymeric cascade prodrug or corresponding linker reagent according to claim 90, wherein Nu represents a nucleophile selected from the group consisting of primary, secondary and tertiary amino groups, thiols, carboxylic acids, hydroxylamines, hydrazine and nitrogen containing heteroaryls.

121. (Previously presented) The polymeric cascade prodrug or corresponding linker reagent according to claim 90, wherein Y_4 represents $-\text{C}(\text{R}_7)(\text{R}_8)$ and at least one of R7 and R8 is not hydrogen.

122. (Currently amended) The polymeric cascade prodrug or corresponding linker reagent according to claim 90, wherein Ar represents a structure selected from the group consisting of:



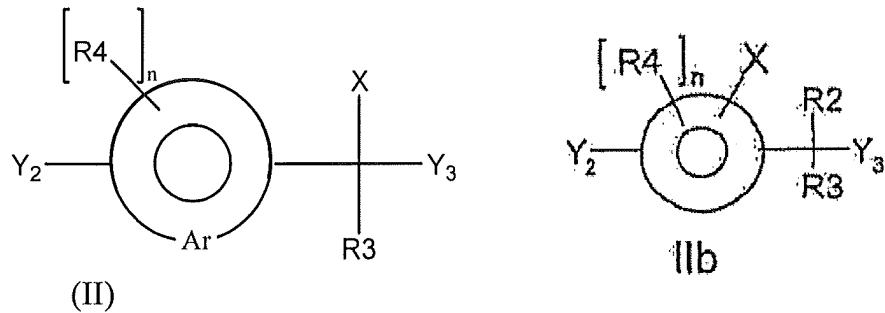
wherein each W independently represents O, S, or N.

123. (Previously presented) The polymeric cascade prodrug or corresponding linker reagent according to claim 90, wherein Ar represents a monocyclic or dicyclic aromatic hydrocarbon or aromatic heterocycle.

124. (Previously presented) The polymeric cascade prodrug or corresponding linker reagent according to claim 90, wherein the Ar represents a five-membered or six-membered aromatic hydrocarbon or aromatic heterocycle.

125. (Previously presented) A method for synthesizing a polymeric prodrug, the method comprising:

(a) providing a starting molecule corresponding to the general Formula II or IIb:



(b) reacting the starting molecule with a masking group having a nucleophile to form at least one intermediate compound wherein the masking group is bound to Y₂; and

(c) reacting an amine-containing biologically active moiety D with the at least one intermediate compound to form a polymeric prodrug is formed;

wherein Y₂ is selected from O, S, or NR₆; Y₃ is selected from O or S; X is a spacer moiety; R₃ is selected independently from hydrogen, substituted or non-substituted linear, branched or cyclical alkyl or heteroalkyl, aryl, substituted or non-substituted heteroaryl, cyano nitro, halogen, carboxy, carboxyalkyl, alkylcarbonyl or carboxamidoalkyl; R₄ is selected from hydrogen, substituted or non-substituted linear, branched or cyclical alkyl or heteroalkyl, aryl, substituted aryl, substituted or non-substituted heteroaryl, substituted or non-substituted linear, branched, or cyclical alkoxy, substituted or non-substituted linear, branched, or cyclical heteroalkyloxy, aryloxy or heteroaryloxy, cyano, or halogen; R₆ is selected from hydrogen, substituted or non-substituted linear, branched or cyclical alkyl or heteroalkyl, aryl, substituted aryl substituted or non-substituted heteroaryl; and Y₆ is O, S, NR₆, succinimide, maleimide, unsaturated carbon-carbon bonds or a heteroatom containing a free electron pair; n is zero or a positive integer and Ar is a multi-substituted aromatic hydrocarbon or a multi-substituted aromatic heterocycle.

126. (Previously presented) A method for hydrolyzing a polymeric cascade prodrug or corresponding linker reagent according to claim 89, comprising providing the prodrug or

corresponding linker reagent and placing the prodrug or corresponding linker reagent in a solution with a pH of approximately 7.4.

127. (Previously presented) A method of administering an amine-containing moiety to an organism in need thereof, the method comprising providing a polymeric cascade prodrug according to claim 89, administering the polymeric cascade prodrug to the organism and cleaving the amine-containing moiety from the polymeric cascade prodrug by means of a substantially non-enzymatic reaction.

128. (Previously presented) A method of providing a therapeutically useful concentration of a biologically active molecule by *in vivo* cleavage of the biologically active molecule from the prodrug according to claim 89.